

CLMPTO 10/21/04 SLW

1. A secondary or three-dimensional structure of a purified glycosyltransferase when it associates with a nucleotide sugar donor, acceptor, or metal cofactor.
2. A secondary or three-dimensional structure of a purified glycosyltransferase in association with a moiety.
3. A secondary or three-dimensional structure as claimed in claim 2, wherein the moiety is a nucleotide sugar donor, acceptor, metal cofactor, or heavy metal atom.
4. (Amended) A secondary or three-dimensional structure of a glycosyltransferase as defined in claim 1 that is a crystalline form.
5. (Amended) A secondary or three-dimensional structure of a glycosyltransferase as defined in claim 1, wherein the glycosyltransferase is an N-acetylglucosaminyltransferase.
6. (Amended) A secondary or three-dimensional structure of a glycosyltransferase as defined in claim 1 having one or both of the following characteristics:
 - (a) a N-terminal domain comprising an eight-stranded mixed β -sheet flanked by six helices, and a small two-stranded antiparallel β -sheet ; and
 - (b) a C-terminal domain comprising a four-stranded mixed β -sheet flanked by three α -helices and a short β -finger.
7. A secondary or three-dimensional structure of a glycosyltransferase as defined in claim 6 further characterized by the N-terminal domain and C-terminal domain being connected by a linker region which wraps halfway around the N-terminal domain before starting the first helix of the C-terminal domain.
8. (Amended) A secondary or three-dimensional structure of a glycosyltransferase as defined in claim 1 having the structural coordinates of a glycosyltransferase listed in Table 1, 2, 3, or 4.

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9. A secondary or three-dimensional structure of a glycosyltransferase in association with a sugar nucleotide donor having the structural coordinates of a glycosyltransferase and a sugar nucleotide donor listed in Table 3.
10. A secondary or three-dimensional structure of a glycosyltransferase in association with an acceptor having the structural coordinates of a glycosyltransferase and an acceptor listed in Table 4.
11. A crystalline form of a glycosyltransferase having a unit cell with dimensions of $a = 40.4 \pm 3 \text{ \AA}$, $b = 82.4 \pm 3 \text{ \AA}$, and $c = 102.5 \pm 3 \text{ \AA}$.
12. A crystalline form of an N-acetylglucosaminyltransferase having the structural coordinates listed in Table 1, 2, 3, or 4, and a unit cell with dimensions of $a = 40.4 \pm 3 \text{ \AA}$, $b = 82.4 \pm 3 \text{ \AA}$, and $c = 102.5 \pm 3 \text{ \AA}$.
13. (Amended) A crystalline form as claimed in claim 11 further characterized by the parameters, diffraction statistics, and/or refinement statistics in Table 6.
14. (Amended) A secondary or three-dimensional structure of a binding site of a secondary or three-dimensional structure of a glycosyltransferase as defined in claim 1.
15. A secondary or three-dimensional structure of a binding site as claimed in claim 14 wherein the binding site is defined by its association with one or more of a diphosphate group of a sugar nucleotide donor, a nucleotide of a sugar nucleotide donor, a sugar of a nucleotide of a sugar nucleotide donor, a selected sugar of a sugar nucleotide donor that is transferred to an acceptor, and/or an acceptor.

16. (Amended) A secondary or three-dimensional structure of a binding site of a glycosyltransferase as defined in claim 1 wherein the binding site is also defined by the atomic interactions of Table 5, preferably the enzyme atomic contacts.
17. (Amended) A secondary or three-dimensional structure of a binding site of a glycosyltransferase as defined in claim 1 wherein the binding site is defined by atomic interactions 1 to 5; 6 and 7; 8, 9 and 10; 1 to 13; 14 to 21; 22 to 27; 1 to 13; 1 to 21; or 11, 12, 13, and 27 listed in Table 5, or the enzymic atomic contacts for these atomic interactions listed in Table 5.
18. (Amended) A secondary or three-dimensional structure of an spsA GnT I core (SGC) domain of a secondary or three-dimensional structure of a glycosyltransferase as defined in claim 1.
19. A secondary or three-dimensional structure of an SGC domain as claimed in claim 18 characterized by an eight-stranded mixed β -sheet, flanked by six helices, and a small two-stranded antiparallel β -sheet.
20. (Amended) A modulator of the activity of a glycosyltransferase derived from a secondary or three-dimensional structure as claimed in claim 1.
21. A method of determining three-dimensional structures of polypeptides with unknown structure comprising the step of applying the structural coordinates of Table 1, 2, 3, or 4.
22. A method for identifying a potential modulator of a glycosyltransferase, or binding sites or domains thereof, comprising the step of using the structural coordinates of Table 1, 2, 3, or 4 that define a glycosyltransferase or binding sites or domains thereof, to computationally evaluate a test compound for its ability to associate with the glycosyltransferase, binding sites or domains thereof, wherein a test compound that associates is a potential modulator of a glycosyltransferase.

23. (Amended) A method for identifying a modulator of a glycosyltransferase by determining binding interactions between a test compound and secondary or three-dimensional structures of binding sites as defined in claim 1 comprising:

(a) generating the binding sites on a computer screen;

(b) generating a test compound with its spatial structure on the computer screen;

and

(c) testing to determine whether the test compound binds to a selected number of binding sites.

24. (Amended) A method for identifying a potential modulator of a glycosyltransferase function comprising the steps:

- (a) docking a computer representation of a compound from a computer data base with a computer representation of a secondary or three-dimensional structure of a glycosyltransferase or a binding site as defined claim 1, to obtain a complex;
- (b) determining a conformation of the complex with a favourable geometric fit and favourable complementary interactions; and
- identifying compounds that best fit the selected site as potential modulators of the glycosyltransferase.

25. (Amended) A method for identifying a potential modulator of a glycosyltransferase function comprising the steps:

- (a) modifying a computer representation of a compound complexed with a secondary or three-dimensional structure of a glycosyltransferase or a binding site as defined in claim 1, by deleting or adding a chemical group or groups;
- (b) determining a conformation of the complex with a favourable geometric fit and favourable complementary interactions; and
- (c) identifying a compound that best fits the binding cavity as a potential modulator of a glycosyltransferase.

26. (Amended) A method for identifying a potential modulator of a glycosyltransferase function comprising the steps:

- (a) selecting a computer representation of a compound complexed with a secondary or three-dimensional structure of a glycosyltransferase or a binding site as defined in claim 1; and
- (b) searching for molecules in a data base that are similar to the compound using a searching computer program, or replacing portions of the compound with similar

chemical structures from a data base using a compound building computer program.

27. (Amended) A modulator of a glycosyltransferase identified by a method as claimed in claim 1.
28. (Amended) A method for designing potential inhibitors of a glycosyltransferase comprising the step of using the structural coordinates of a sugar nucleotide donor or acceptor or component thereof, defined in relation to its spatial association with the three dimensional structure of a glycosyltransferase or a binding site as defined in claim 1, to generate a compound that is capable of associating with the glycosyltransferase or binding cavity thereof.
29. (Amended) A modulator of a glycosyltransferase based on a three-dimensional structure of a sugar nucleotide donor, an acceptor, or a component thereof, defined in relation to the sugar nucleotide donor's or acceptor's spatial association with a secondary or three-dimensional structure of a glycosyltransferase or binding site as defined in claim 1.
30. (Amended) A pharmaceutical composition comprising a modulator as claimed in claim 1 either alone or with other active substances.
31. A method of treating a disease associated with a glycosyltransferase with inappropriate activity in a cellular organism, comprising:
 - (a) administering a pharmaceutical composition as claimed in claim 30; and
 - (b) activating or inhibiting a glycosyltransferase to treat the disease.
32. (Amended) Use of a modulator identified by the methods of claim 1 in the preparation of a medicament to treat a disease associated with a glycosyltransferase with inappropriate activity in a cellular organism.
33. Use of structural coordinates of a glycosyltransferase structure as set out in Table 1, 2, 3, or 4 to manufacture a medicament.

34. (Amended) Machine readable media encoded with data representing the structural coordinates of a secondary or three-dimensional structure of a glycosyltransferase or a binding site as defined in claim 1.
35. A machine readable media as claimed in claim 34 wherein the data also includes structural coordinates for a nucleotide sugar donor, acceptor, metal cofactor, or heavy metal atom.